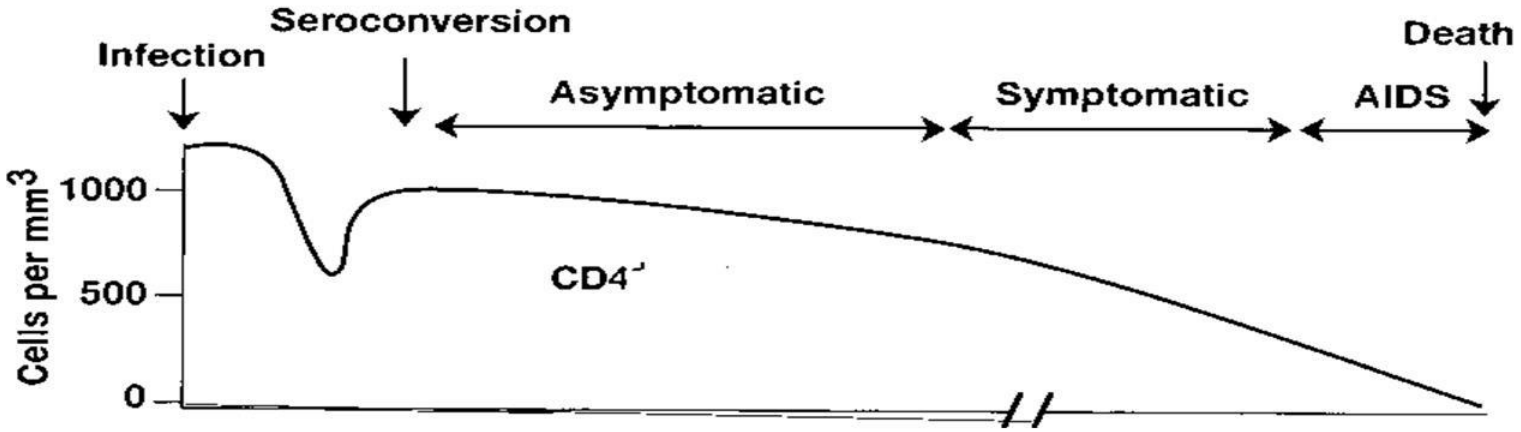
HIV / AIDS



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Objectives-

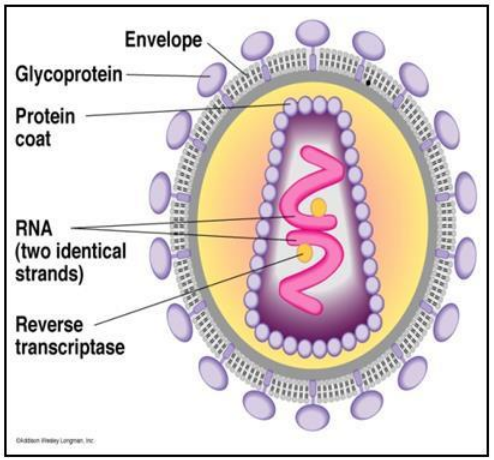
By the end of the lecture you will be able to :

- Define and understand the difference between HIV Infection and AIDS
- Describe the progression of HIV from initial infection to disease
- Determine the clinical picture of HIV/AIDS patient
- Understand the modes of transmission of HIV Describe ways to prevent HIV infection
- Discuss issues relating to HIV testing

- **Reference book : Kumar & Clark's clinical medicine . 8th edition . Page 171- 194**

What is HIV/AIDS?

- **HIV,** Human Immunodeficiency Virus, **is a global pandemic and the number of people living with HIV continues to increase worldwide.**
- It is preventable & manageable but is NOT curable.
- is a unique type of virus (a retrovirus) .
- This virus causes HIV infection and AIDS , Acquired Immunodeficiency Syndrome.
- The HIV infected person may, or may not have AIDS. When the immune system becomes weakened by HIV, the illness progresses to AIDS.



Structure of the HIV is a Retrovirus, which has reverse transcriptase enzyme that transcribe RNA into DNA after entering a cell . This unique character allows the incorporation of the virus into human genome

AIDS

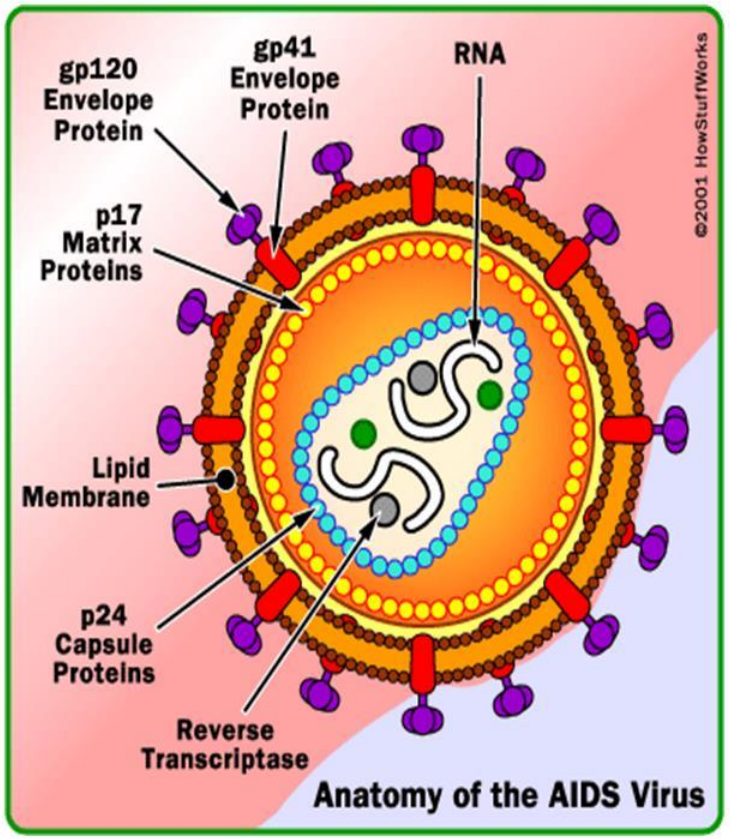
- AIDS is the final stage of HIV disease.

- AIDS emergence was in 1981 of a cluster of diseases associated with progressive failure of cellular immunity, which allows life-threatening opportunistic infections and cancers to thrive, in adults who had no obvious reason for presenting such immune deficiencies.
- Opportunistic infections and malignancies that rarely occur in the absence of severe immunodeficiency (e.g. Pneumocystis pneumonia, central nervous system lymphoma).

- Persons with positive HIV serology who have ever had a CD4 lymphocyte count below 200 cells/ mm^3 or a CD4 lymphocyte percentage below 14% are considered to have AIDS.

Viral Genome

- Lentivirus subfamily of ***retroviruses.***
- Retroviruses transcribe RNA to DNA.
- Two viral strands of RNA found in core protein (P24) surrounded by protein outer coat (P17).
- Outer envelope glycoprotein (P120) contains a lipid matrix within which specific viral glycoproteins are imbedded.
- These knob-like structures responsible for binding to target cell (Helper T cells - CD4 cells).

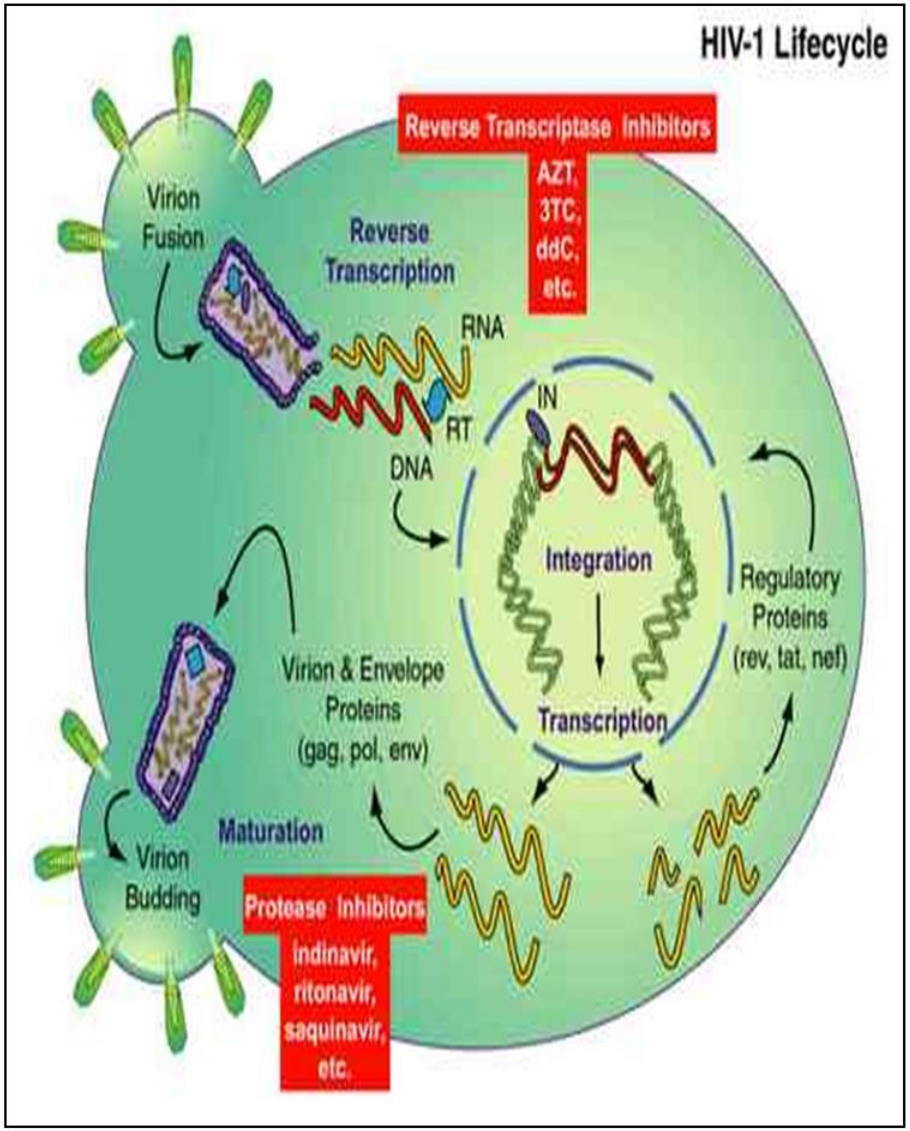


HIV-1 and HIV-2

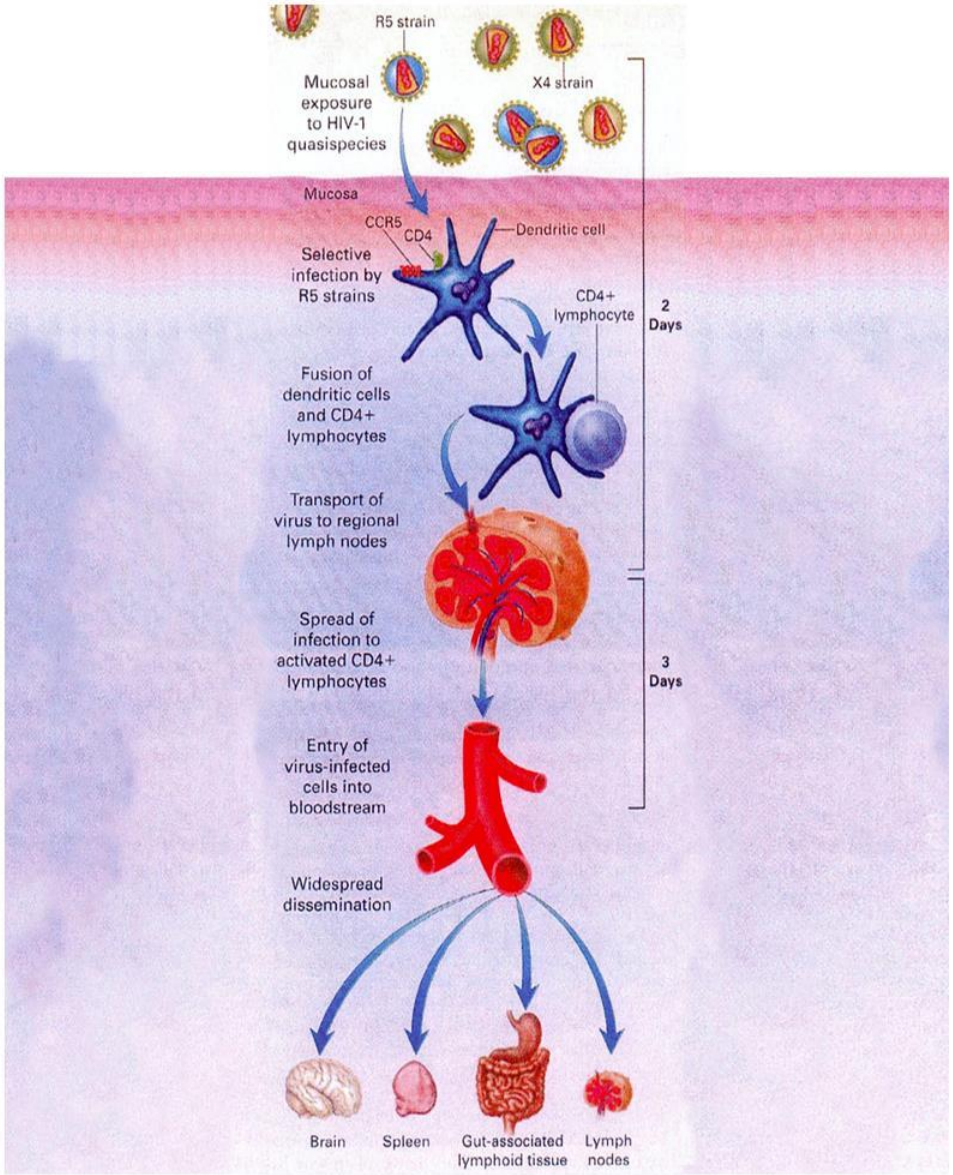
- HIV-1 and HIV-2, have similar epidemiological characteristics.
- HIV-1 is the most frequent occurring strain globally.
- HIV-2 has more indolent course, less pathogenicity, than HIV-1.
- Many drugs that are used in HIV-1 are ineffective in HIV-2
- Lower rates of mother to child transmission for HIV-2.

Immunopathogenesis of HIV

- **HIV multiplies inside the resting CD4+ cells** (T lymphocyte)
- The virus uses the genetic mechanisms of the cell to produce millions of new viruses
- Acute Infection: wide dissemination of HIV into lymphoid tissue with establishment of chronic persistent infection
- loss of CD4+ cells immunodeficiency **with increase the viral load**
- **HIV-infected people become vulnerable to opportunistic infections** or AIDS related cancers.



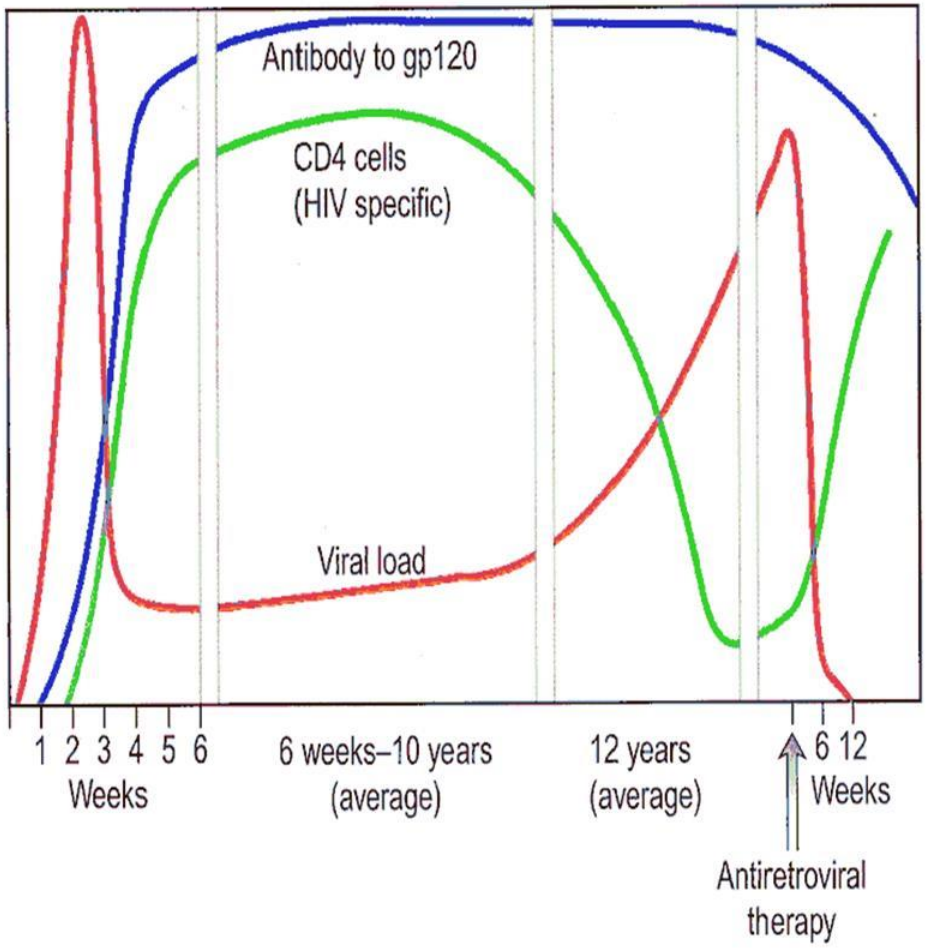
Which Body Fluids Contain HIV?



- HIV lives and reproduces in blood and other body fluids as Semen, Breast milk, Vaginal fluids, Rectal mucous.
- While the virus has occasionally been found in saliva, tears, urine and bronchial secretions, transmission after contact with these secretions has not been reported.
- Healthcare workers may be exposed to some other body fluids with high concentrations of HIV, including: Amniotic fluid, CSF, Synovial fluid

Immune response to HIV

- **Incubation period** : variable .
- Although the time from infection to the development of detectable antibodies is generally 1–3 months, the time from HIV infection to diagnosis of AIDS has an observed range of less than 1 year to 15 years or longer.
- **Window period** : antibody to HIV may be absent during the early stage of infection, although high level of viral RNA – P24 core protein which – detected by HIV NAAT assay.
- CD4 gradually depleted with disease progression & high level of viral RNA.
- CD4:CD8 ratio reversed.



Virus can be transmitted during each stage

Natural course of HIV disease

- **Seroconversion & 1ry illness:**
  - Infection with HIV, antibodies develop
- **Asymptomatic (Clinical latency)**
  - No signs of HIV, immune system controls virus production
- **Symptomatic HIV inf :**
  - Physical signs of HIV infection, some immune suppression
- **AIDS:**
  - Opportunistic infections with very low virulent infections, end-stage disease

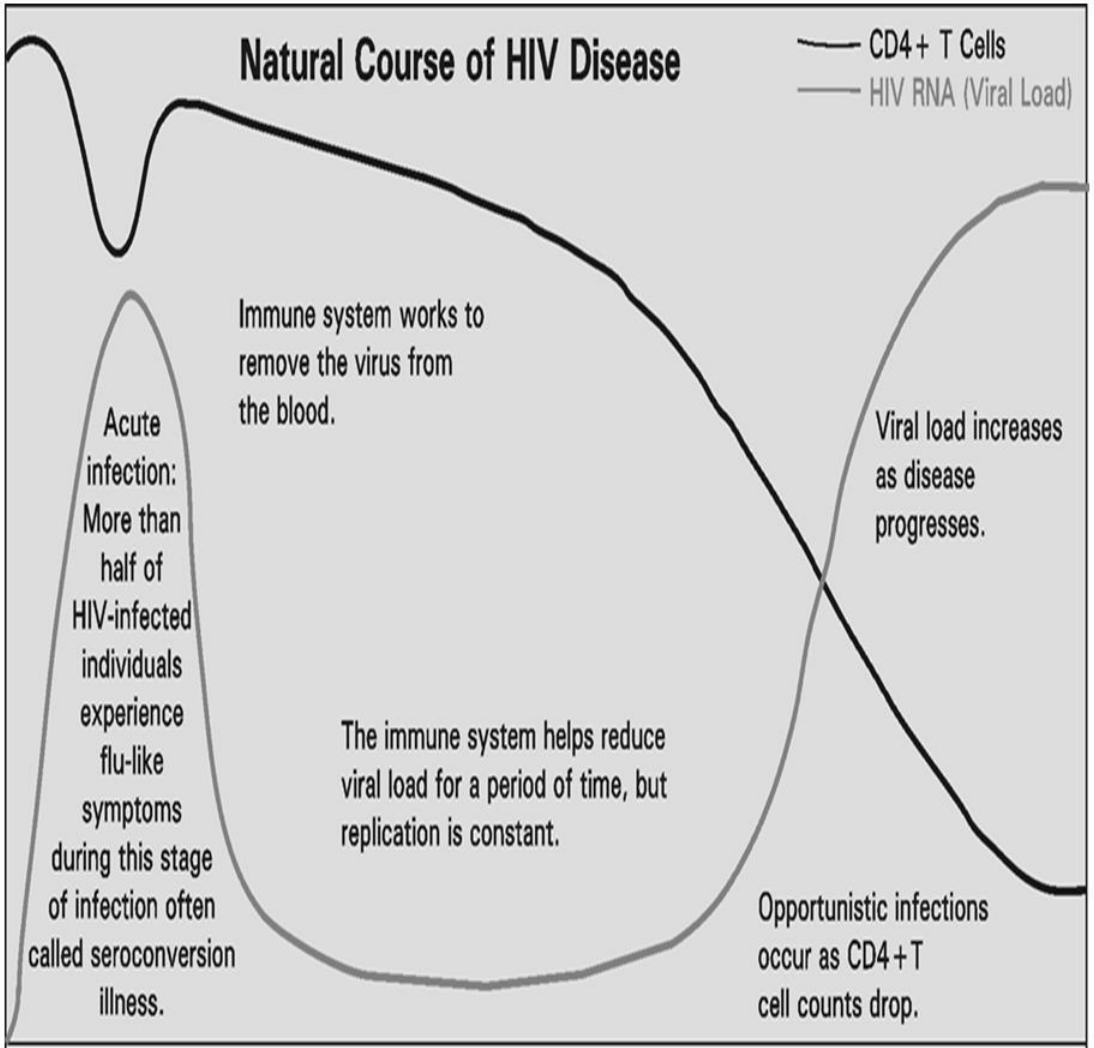


Figure1. The natural progression of HIV disease. Without intervention, viral load will continue to increase as CD4+T cell counts decline.

Virus can be transmitted during each stage

Clinical Manifestations of HIV Infection

- Transmission
- Acute (primary) HIV Infection
- Asymptomatic HIV Infection
- Symptomatic HIV Infection (thrush, diarrhea)
- AIDS: Opportunistic Infections, Cancers, Neurologic Disease

Mode of HIV Transmission

- Blood transmission (contaminated transfusions, needle sharing, needle-stick)
- vertical transmission (mother to child)
- sexual transmission (75% infections worldwide)

Mode of transmission (cont.)

- After direct exposure of health care workers to HIV-infected blood through injury with needles and other sharp objects, the rate of seroconversion is less than 0.5%, much lower than the risk of hepatitis B virus infection after similar exposures (about 25%).
- Unsafe injections may account for up to 5% of transmission.

- No laboratory or epidemiological evidence suggests that biting insects have transmitted HIV infection.

Progression of HIV Infection

- Severity of illness is determined by amount of virus in the body (increasing viral load) and the degree of immune suppression (decreasing CD4+ counts)
- Higher the viral load, the sooner immune suppression occurs

AIDS is diagnosed by the following elements:

- A confirmed positive test for HIV/AIDS *(higher viral load means more immune suppression).*
- LOW CD4 count
- The presence of either an opportunistic infection or AIDS related cancer.

Stage 1 – Acute (Primary) illness

- Short, flu-like illness – occurs 1- 6 weeks after infection.
- Symptoms range from minimal fever, aches, and pains to very severe symptoms.
- Infected person can infect other people

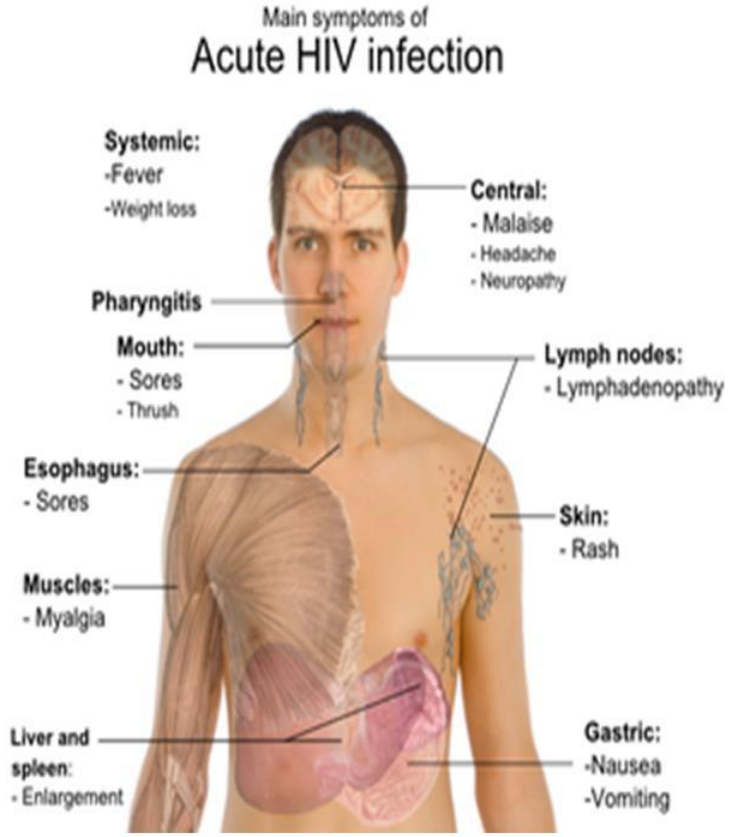


Table 22. Acute Retroviral Syndrome: Associated Signs and Symptoms (Expected Frequency) *[see reference 201]*

- Fever (96%)
- Lymphadenopathy (74%)
- Pharyngitis (70%)
- Rash (70%)
  - ✓ Erythematous maculopapular with lesions on face and trunk and sometimes extremities, including palms and soles.
  - ✓ Mucocutaneous ulceration involving mouth, esophagus or genitals.
- Myalgia or arthralgia (54%)
- Diarrhea (32%)
- Headache (32%)
- Nausea and vomiting (27%)
- Hepatosplenomegaly (14%)
- Weight Loss (13%)
- Thrush (12%)
- Neurologic symptoms (12%)
  - ✓ Meningoencephalitis or aseptic meningitis
  - ✓ Peripheral neuropathy or radiculopathy
  - ✓ Facial palsy
  - ✓ Guillain-Barré syndrome
  - ✓ Brachial neuritis
  - ✓ Cognitive impairment or psychosis

2nd stage – Asymptomatic (Clinical latency)

- Lasts for an average of ten years
- This stage is free from symptoms
- There may be generalized lymphadenopathy
- The level of HIV in the blood drops to low levels
- HIV antibodies are detectable in the blood

3rd stage - Symptomatic

- The immune system deteriorates
- Opportunistic infections and cancers start to appear.

CD4+ Cell Count	Organism	Common Manifestations
> 500 cells/mm^3	HIV	Primary HIV infection
	HIV	Persistent generalized lymphadenopathy
	HIV	Aseptic meningitis
	HIV	Idiopathic thrombocytopenia purpura
< 500 cells/mm^3	*Streptococcus pneumoniae, Haemophilus influenza*	Community-acquired pneumonia
	Mycobacterium tuberculosis	Pulmonary tuberculosis
	Candida species	Oropharyngeal and vaginal candidiasis
	Herpes simplex virus	Orogenital herpes
	Varicella zoster virus	Dermatomal zoster (shingles)
	Epstein-Barr virus	Oral hairy leukoplakia, non-Hodgkin's lymphoma
	Cryptosporidium parvum	Self-limited diarrhea
	HHV-8 (KSHV)	Kaposi's sarcoma

< 200 cells/mm^3	*Pneumocystis carinii*	Pneumonia
	Cryptosporidium parvum	Chronic diarrhea
< 100 cells/mm^3	*Toxoplasma gondii*	Encephalitis
	Microsporidia	Diarrhea
	Candida species	Esophagitis
	Cryptococcus neoformans	Meningitis
	M tuberculosis	Disseminated or extrapulmonary TB
	Herpes simplex virus	Disseminated or aggressive herpes
	Varicella zoster virus	Disseminated herpes zoster
	Epstein-Barr virus	Primary central nervous system lymphoma
	Mycobacterium avium complex	Disseminated *M avium* complex
	Cytomegalovirus	Retinitis, GI disease, encephalitis
	HIV	Wasting syndrome, dementia, myelopathy

4th stage, AIDS

- AIDS is the late stage of HIV infection
- When HIV infection progresses to AIDS, many people begin to suffer from fatigue, diarrhea, nausea, vomiting, fever, chills, night sweats, and even wasting syndrome at late stages.
- The most common AIDS-related cancers are Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer.
- Many of the signs and symptoms of AIDS come from opportunistic infections (very low virulent organism)

Kaposis's sarcoma in AIDS patient

AIDS Associated Disease Categories

1. Gastrointestinal: Cause most of illness and death of late AIDS (diarrhea, infection, wasting …).

2. Respiratory: 70% of AIDS patients develop serious respiratory problems (infection, T.B, cancer …).

3. Neurological: Opportunistic diseases and tumors of central nervous system, and *AIDS dementia complex.*

4. Hematological :

Lymphopenia, Anaemia of chronic disorders, Neutropenia, ITP, Pancytopenia, mylotoxic drugs

5. Skin Disorders: 90% of AIDS patients develop skin or mucous membrane disorders (Kaposi's sarcoma - Most common type of cancer in AIDS patients)

6. 6. Eye Infections: 50-75% patients

Centers for Disease Control and Prevention (CDC) Classification

CDC Classification System for HIV-Infected Adults and Adolescents

CD4 Cell Count Categories	Clinical Categories		
	A Asymptomatic, Acute HIV, or PGL	**B** Symptomatic Conditions, not A or C	**C** AIDS-Indicator Conditions
(1) ≥500 cells/μL	A1	B1	C1
(2) 200-499 cells/μL	A2	B2	C2
(3) <200 cells/μL	A3	B3	C3

Patients in categories A3, B3, and C1-C3 are considered to have AIDS.

Centers for Disease Control and Prevention (CDC)

2008 CDC Case Definition for HIV Infection: AIDS-Defining Clinical Conditions

- Candidiasis (trachea, bronchia, or lung)
- Candidiasis (esophageal)
- Cervical cancer (invasive)
- Coccidioidomycosis (disseminated or extrapulmonary)
- Cryptococcosis (extrapulmonary)
- Cryptosporidiosis (intestinal, for longer than 1 month)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy (HIV-related)
- Herpes simplex: chronic ulcers (present for longer than 1 month)
- Herpes simplex: bronchitis, pneumonitis, or esophagitis
- Histoplasmosis (disseminated or extrapulmonary)
- Isosporiasis (intestinal, for longer than 1 month)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary of brain
- *Mycobacterium avium* complex, disseminated or extrapulmonary
- *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*; any site (pulmonary or extrapulmonary
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Recurrent pneumonia ($\geq$ 2 episodes in 1-year period)
- Progressive multifocal leukoencephalopathy
- Salmonella (recurrent septicemia)
- Toxoplasmosis (brain)
- Wasting syndrome due to HIV: >10% involuntary weight loss plus either chronic diarrhea ($\geq$ 2 stools per day for at least 30 days) or chronic weakness and documented fever (for at least 30 days) in the absence of a concurrent illness or condition other than HIV that could explain this finding.

Testing Options for HIV

- HIV is diagnosed either by detection of viral specific antibodies or by direct identification of viral RNA antigen.
- Detection of IgG antibody to envelope components (P120) or to P24 core protein, using ELISA technique (screening) & western blot (confirmatory).
- Up to 3 months (mean 3 weeks), an HIV infected person may show negative test (serologic latency- window period).
- Genome detection assay – Nucleic acid based assays (RT-PCR).
- Viral P24 antigen which is detectable shortly after infection, usually disappeared by 8-10 weeks after exposure

Blood Detection Tests

HIV enzyme-linked immunosorbent assay (ELISA)	**Screening test for HIV Sensitivity > 99.9%**
Western blot	Confirmatory test Specificity > 99.9% (when combined with ELISA)
HIV rapid antibody test (all body fluid)	Screening test for HIV Simple to perform (home testing)
HIV viral load (HIV RNA)assays: e.g. RT - PCR	Best test for diagnosis of acute HIV infection Correlates with disease progression and response to HAART
Absolute CD4 lymphocyte count	Predictor of HIV progression Risk of opportunistic infections and AIDS when <200

Treatment Options

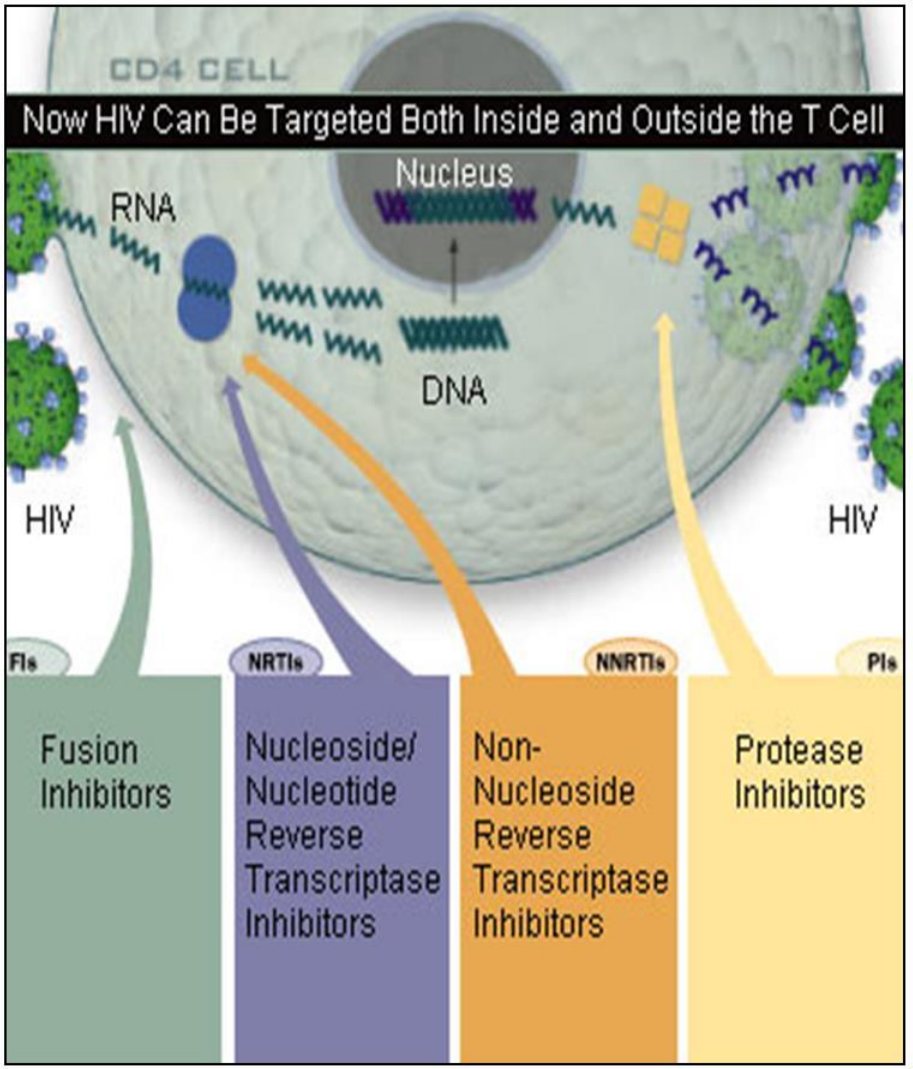
Prevention of HIV Transmission

- **Public health strategies to prevent HIV transmission**
- Screen all blood and blood products

- Abstinence from all HIV related risky behaviors (such as sexual intercourse, sharing of IV needles, body piercing, or tattooing using non sterile needles, etc)is the only 100% effective way to prevent transmission of HIV.

HAART = highly active anti-retroviral treatment

- **Reverse Transcriptase Inhibitors:** **Competitive enzyme inhibitors. Example:** AZT (Zidovudine)
- **Protease Inhibitors:** **Inhibit the viral proteases. Prevent viral maturation. E.g.** Norvir (Ritonavir)
- **Drug combinations**
- **Drug cocktails have been very effective in suppressing HIV replication and prolonging the life of HIV infected individuals, but long term effectiveness is not clear.**



HEALTH CARE FOLLOW UP OF HIV INFECTED PATIENTS

For all HIV-infected individuals:

- CD4 counts every 3–6 months
- Viral load tests every 3–6 months and 1 month following a change in therapy
- T.B detection
- INH for those with positive T.B and normal chest radiograph
- RPR or VDRL for syphilis
- Toxoplasma IgG serology
- CMV IgG serology
- Pneumococcal vaccine
- Influenza vaccine in season
- Hepatitis B vaccine for those who are HBsAb-negative
- *Haemophilus influenzae* type b vaccination
- Papanicolaou smears every 6 months for women